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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,557	07/22/2002	Gerald Juergen Roth	5/1271PCT	3607

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EXAMINER

WRIGHT, SONYA N

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 09/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/069,557	ROTH ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Sonya Wright	1626	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 13-24 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21 and 22 is/are rejected.
- 7) ☒ Claim(s) 13-20, 23 and 24 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All   b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                     | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                            | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>0903</u> . | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

Claims 13-24 are pending in this application.

#### ***Election/Restrictions***

Applicant's election without traverse of the species 3-(Z)-{1-(4-(dimethylaminomethyl)-anilino)-1-phenyl-methylidene}-5,6-dimethoxy-2-indolinone in the response received July 30, 2003 is acknowledged.

The following embodiment has been identified for examination:

Claims 13-24 wherein X, R1, and R2 are as defined; R3 is unsubstituted phenyl; R4 is a hydrogen atom or a C1-3-alkyl group; R5 is a hydrogen atom or a C1-3-aryl group; R6 is as defined; Ra, Rb, Rc, Rd, m, and n are as defined.

All remaining subject matter has been withdrawn from consideration for being drawn to non-elected subject matter. The withdrawn subject matter of claims 13-24 is properly restricted as said subject matter differs in structure and element from the elected subject matter so as to be patentably distinct therefrom, i.e. a reference which anticipated the elected subject matter would not even render obvious the withdrawn subject matter and fields of search are not co-extensive.

Claims 13-24 are objected to as containing non-elected subject matter. This objection may be overcome by limiting the claims to the elected subject matter identified *supra*.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

- 1) Nature of invention.
- 2) State of prior art.
- 3) Level of ordinary skill in the art.
- 4) Level of predictability in the art
- 5) Amount of direction and guidance provided by the inventor.
- 6) Existence of working examples.
- 7) Breadth of claims.
- 8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

1) Nature of the invention.

Claim 21 is directed to “a method of treating excessive or anomalous cell proliferation”. Claim 22 is drawn to a method of “treating tumours”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

2) State of the prior art.

The prior arts do not indicate that the instant compound is useful in treating all forms of “excessive or anomalous cell proliferation” and “tumours”. Applicant cites L. Mengtao in J.Virology 71 (3), 1984-1991 (1997) regarding viral cyline. Applicant cites background references regarding “anomalous cell proliferation” and “tumours” in page 33, last paragraph and page 34, first paragraph.

3) Level of ordinary skill in the art.

There are a vast number of diseases caused by “excessive or anomalous cell proliferation” and a vast number of “tumours”. Applicant does not give support for treating all forms of diseases caused by “excessive or anomalous cell proliferation” and all forms of “tumours”. In page 33, last paragraph, Applicant indicates that the proliferation of endothelial cells and the concomitant neovascularisation constitute a crucial stage in tumour progression, and that furthermore, the proliferation of endothelial cells is also important in haemangiomas, in metastatisation, rheumatoid arthritis, psoriasis and ocular neovascularisation. The level of ordinary skill in the art is high.

4) Level of predictability in the art.

The various forms of diseases caused by “excessive or anomalous cell proliferation” and the various forms of “tumours” have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. The art pertaining to diseases caused by “excessive or anomalous cell proliferation” and “tumours” remains highly unpredictable.

5) Amount of direction and guidance provided by the inventor.

Applicant provides limited guidance regarding biological activity on pages 31-35. Applicant provides data from a biological test with Human umbilical endothelial cells (HUVEC). In the test, the proliferation of the cells was stimulated and the compounds according to the invention were added to the cultures. The relative cell proliferation was calculated as a percentage of the control and the concentration of active substance which inhibits the proliferation of the cells by 50% was determined. The Table on page 33 gives the results.

6) Existence of working examples.

There are limited working examples which do not support that the instant compounds are useful in treating all forms of "excessive or anomalous cell proliferation" or all forms of "tumours". Applicant provides the data from a biological test of the inhibitory effects of the instant compounds on page 33. The third paragraph on page 33 indicates that the instant compounds have an inhibitory effect on the proliferation of cells, particularly endothelial cells and tumour cells.

7) Breadth of claims.

Claim 21 is extremely broad due to the large number of diseases caused by "excessive or anomalous cell proliferation" and the large number or types of "tumours". Applicant has not shown that the instant compounds are useful in treating all forms of diseases caused by "excessive or anomalous cell proliferation" or all forms of "tumours".

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

To overcome this rejection, it is suggested that Applicant list in claims 21 and 22, specific diseases which are identified in the specification as being treatable by the instant compounds.

### ***Specification***

The disclosure is objected to because of the following informalities:

The disclosure does not make reference to the continuing data. Therefore, it is requested that Applicant insert the following statement at the beginning of the specification, after the title: --This application is a 371 of PCT/EP00/08149 filed August 22, 2000.--

Appropriate correction is required.

The reference cited on the PTO-892 is included only to show the state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

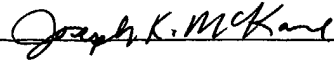
Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.



Application/Control Number: 10/069,557  
Art Unit: 1626

Page 8

A handwritten signature in black ink, reading "Joseph K. McKane", is positioned above a horizontal line.

Joseph K. McKane

Supervisory Patent Examiner

Group 1600

Sonya Wright

September 5, 2003